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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,211	12/05/2001	Milton D. Goldenberg	IMMU:003US1	5605

37013 7590 02/25/2010

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EXAMINER
DAHLE, CHUN WU

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
02/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ptomail@rkmlegalgroup.com

Office Action Summary	Application No.	Applicant(s)	
	10/002,211	GOLDENBERG, MILTON D.	
	Examiner	Art Unit	
	CHUN DAHLE	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-86 and 93-116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78-86 and 93-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to the claims, filed on October 15, 2009, is acknowledged.

Claims 114-116 have been added.

Claims 1-77 and 87-92 have been previously canceled.

Claims 78-86, 93-113, and newly added claims 114-116 are pending and currently under consideration as they read on the originally elected species of a method of treating immune thrombocytopenic purpura (ITP) and LL2 antibody.

2. This Office Action will be in response to applicant's arguments, filed on October 15, 2009.

The rejections of record can be found in the previous Office Action, mailed on August 17, 2006, March 9, 2007, and July 26, 2007, April 23, 2008, and April 15, 2009.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 78-86, 93-113, and newly added claims 114-116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

The following *written description* rejection is set forth herein.

Applicant's arguments, filed on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant argues that the claims have been amended to narrow the scope from "a B-cell antibody or fragment thereof" to "a B-cell antibody or fragment thereof, which specifically binds to a B-cell". Thus, applicant asserts that the claimed methods only encompass B-cell antibody that binds to B-cell surface proteins. As such, applicant argues that the single species of anti-CD22 antibody is sufficient to satisfy the genus anti-B cell antibody encompassed by the claimed method of ablating normal cells.

This is not fund persuasive for following reasons:

Applicant has claimed a method of ablating normal cells in a subject and/or a method of treating an immune disease by administering a therapeutically effective amount of a composition comprising a B-cell antibody or fragment thereof wherein the antibody specifically binds to a B-cell, thereby to ablate the normal cells.

The specification does not provide adequate written description support for the broad genus of antibodies encompassed by the claimed language.

The specification discloses that treatment of ablation of certain normal organs and tissues by using a growth factor receptor antibody or a hormone receptor antibody to target end-organ bearing such receptors (e.g. see page 7). The ablation method dose not describe any B-cell antibody or fragment thereof.

Page 9 of the instant specification discloses ablation using organ and tissue targeting antibodies of certain normal cells and tissues as part of another therapeutic strategy in the cytotoxic ablation of the spleen in patients with immune thrombycytopenic purpura. Again, the ablation methods do not disclose what B-cell antibody or fragment thereof being used.

Page 12 of the specification discloses antibody and fragment thereof that is specific for B-cells including LL2 directed against normal and malignant B-cells that can be used for treating normal spleen cells in patient with immune disease, lymphoma and other disease. The disclosure of LL2 antibody is not in the context of immune thrombycytopenic purpura as claimed in claim 79 (also elected invention).

The disclosure only describes single species of LL2 antibody that binds normal and malignant B-cells (see page 12 of the specification).

The claims is directed to a method of ablating normal cells and/or a method of treating an immune disease in a subject by administering a B cell antibody or fragment thereof which specifically binds to a B cell. The claim is generic in the sense that it includes antibody that binds any proteins of a B cell. Contrary to applicant's assertion that the claims are only limited to antibody that binds B cell surface molecules, it is not clear how the recited "B-cell antibody .... which specifically binds to a B-cell" would only encompass those antibodies that bind to B cell surface since a B-cell would include the surface molecules as well as intracellular molecules. Even *assuming arguendo* that the claims were now limited only to antibody that binds to B-cell surface molecules, the specification fails to provide sufficient description to convey to one of skill in the art that applicant is in possession of the genus of the antibody that binds a B-cell surface proteins for the claimed method. The single monoclonal antibody LL2 described in the specification is insufficient to represent the genus of the monoclonal antibodies required to practice the claimed ablation method in a subject. There is ample evidence of record that the specificities of anti-B cell antibodies falling within the scope of the genus and the structure of the antigens they bind would be expected to vary substantially. For example, Youinou et al. (Autoimmunity Reviews 2006 5:215-221, reference on PTO-892 mailed on August 17, 2006) B-cells express a variety of different cell surface markers depending on the B-cell subsets and locations (e.g. see Table 1 on page 217). In addition, as evidenced by Sees et al. (EP 0739980, reference of record, see page 3 in particular), a mammalian cell (e.g. B cell) may contain up to 30,000 different mRNA sequences that

can be translated to proteins. Thus, the single antibody LL2 described in the specification is insufficiently representative to provide adequate written descriptive support for the genus of antibodies required to practice the claimed method.

Apart from the lack of representative number of species for the broadly claimed genus of "a B-cell antibody which specifically binds to a B-cell", the specification does not provide sufficient relevant identifying characteristics such as complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics of the claimed B-cell antibody.

Applicant maintains that the members of the genus of the antibodies that specifically binds a B-cell share the same function - they each binds to a B cell. Once again, the fact that antibodies bind B cell surface antigen is not considered relevant identifying characteristics that couple with a known or disclosed correlation between function and structure of the broadly diverse antibodies (e.g. antigen specificity) employed in the claimed methods because B cell surface antigens encompass diverse group of proteins with different structure and function as evidenced by Youinou et al. (e.g. see discussion, supra). Even if all of the genus of B-cell antibody can be made, not all of the B-cell antibodies can be used in the claimed method of ablating normal cells and/or treating an immune disease. It is not clear that which of the known monoclonal antibodies that react with human B lymphocytes taught in Table 1 of Kenneth et al. (Blood 1986, 68:1:1-31, reference relied upon by applicant in Remarks filed on November 30, 2007, December 26, 2007, and February 4, 2008) can be used to administer to ablate normal cells and/or to treat an immune disease including immune thrombocytopenic purpura. For the purpose of satisfying the written description requirement, it is not enough merely to refer to a known LL2 antibody and any antibodies that bind to a B-cell being able to practice the claimed *in vivo* method of ablating normal cells and/or treating an immune disease.

Again, neither the exemplary embodiments nor the specification's general method appear to describe structural features, in structural terms that are common to the genus. That is, the specification provides neither a representative number of species (B-cell antibody or fragments thereof) to describe the claimed genus, nor a description of structural features that are common to species (B-cell antibody or fragments thereof). The specification provides no structural description of B-cell antibody other than the one specifically exemplified (LL2 antibody); in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed B-cell antibodies looks like. The specification's disclosure is inadequate to describe the claimed genus of B-cell antibodies. Further, there is no described or art-recognized correlation or relationship between the structure of the invention, the B-cell antibody and its treatment of immune diseases, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of B-cell antibodies which retain the features essential to the instant invention.

As such, applicant is not in possession of the claimed method of ablating normal cells in a subject by administering a "B cell antibody or fragment" thereof which specifically binds to a B cells.

Applicant's arguments have not been found persuasive.

5. Claims 93, 97-100, and 106-108 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

It is noted that claims 106 and 108 are dependent upon claim 93 which encompasses "a B-cell antibody or fragment thereof …… wherein the antibody or fragment thereof is a polyclonal, chimeric or hybrid antibody which binds multiple

epitopes or antigens". Claims 106 and 108 were inadvertently omitted in the previous Office Action mailed on April 15, 2009. The Examiner apologizes for any inconvenience regarding this matter.

The claims recite "a B-cell antibody or fragment thereof …… wherein the antibody or fragment thereof is a polyclonal, chimeric or hybrid antibody which binds multiple epitopes or antigens" as part of the invention.

Applicant's arguments, filed on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant asserts that the specification has verbal support for whole immunoglobulin of any class, chimeric or hybrid antibody with dual or multiple antibody or epitope specificities, and polyclonal antibody. Thus, applicant argues that the skilled artisan would understand that the claimed chimeric or hybrid antibody would bind more than one epitope of CD22 or multiple B cell antigens. As such applicant asserts that the specification provides adequate written description support for the claimed invention.

This is not found persuasive for following reasons:

In contrast to applicant's assertion, given that there is insufficient written description in the specification as-filed regarding "B-cell antibody" for reasons discussed above, applicant is not in possession of any B-cell antibody that has additional antigen specificities (e.g. chimeric or hybrid). Once again, single reference to LL2 antibody is insufficient to provide adequate written description support for "a B-cell antibody" for reasons stated above, let alone written description support for a B cell antibody that binds additional undefined antigens or epitoptes.

6. Claims 102 and 105 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

This is a *Written Description*, New Matter rejection.

The term "B-cell immune disease" recited in claims 102 and 105 is not supported by the original disclosure or claim as filed.

Applicant maintains that page 12 of the specification discloses LL2 targets B cells is useful to treat immune disease. Thus, applicant asserts that the term "B-cell immune disease" is supported by the instant specification.

This is not found persuasive for following reasons:

The specification only discloses "immune disease" (see page 12 of the specification or see below)

> *"Antibodies that target the spleen well include the LL2 (also known as EPB-2) monoclonal antibody, disclosed in Pawlak-Byczkowska, cancer Research, 49:4568-4577 (1989), which is directed against normal and malignant B-cells, and which can be used for treating normal spleen cells in patients* ***with immune diseases, lymphoma, and other diseases****"*

The instant claims now recite "B-cell immune disease" which is not clearly disclosed in the specification. Therefore, the claims represent a departure from the specification and claims originally filed. Applicant's reliance on generic disclosure (an immune disease) do not provide sufficient direction and guidance to the features currently claimed.

Therefore, applicant's arguments have not been found persuasive.

7. This is a **New Ground of Rejection** necessitated by applicant's amendment to the claims. Newly added claims 114-116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a *Written Description*, New Matter rejection.

The term "a marker associated with a B cell" recited in newly added claims 114-116 is not supported by the original disclosure or claims as filed.

The term was rejected on the record under the same ground as new matter in the Office Action mailed on August 17, 2006. The rejection was withdrawn after applicant canceled the limitation in the claims (see Office Action mailed on July 26, 2007).

Applicant's amendment, filed on October 15, 2009, directs support to the paragraph next to the last paragraph in the specification.

The paragraph relied upon by applicant discloses:

"It will be understood that the invention is not limited to use of known antibodies or markers, but can be practiced with antibodies to any marker produced by or associated with an organ or tissue"

Clearly, the specification as filed does not provide sufficient written description of the above-mentioned "limitation". The specification does not provide sufficient support for a marker associated with a B cell. The specification only disclose antibody to any markers the instant claims now recite any antibody specific to a marker associated with a B cell, which were not clearly disclosed in the specification. Therefore, the claims

represent a departure from the specification and claims originally filed. Applicant's reliance on generic disclosure of antibodies and possibly a single or limited species do not provide sufficient direction and guidance to the features currently claimed (antibody specific for a marker associated with a B cell). It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679 683 (CCPA 1972) and MPEP 2163.05.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02, 2163.05-06 and 2173.05 (i).

8. Claims 78-86, 93-113, and newly added claims 114-116 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

Applicant's arguments, filed on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant maintains that Lym-1 and Lym-2 antibodies taught by Meyer are not B-cell antibodies, but are HLA-DR antibodies that bind only at low levels of normal B cells. Applicant argues that Meyer et al. (US Patent 4,861,579, reference of record) show that Lym-1 and Lym-2 antibodies not only bind B-cells but also some solid tumors. Applicant asserts that one of skill in the art would not select Lym-1 and Lym-2 for the claimed methods because these antibodies would not be considered B-cell antibodies. Applicant asserts that the instant claims are enabled since they require a B-cell antibody that specifically binds to a B cell.

This is not found persuasive for following reasons:

In contrast to applicant's assertion, the recitation of "a B-cell antibody.... which specifically binds to a B-cell" does not limit the claims to only antibody exclusively binds B cells. In addition, the specification does not provide sufficient guidance and direction as to how to make the claimed B-cell antibody. The specification discloses only generic methods of making antibody by using whole cell or cell extract as antigen. For example, the specification discloses isolation of cell membrane or intracellular antigens to be used to immunize animals to make antibody (e.g. see page 11 of the instant specification). In fact, the specification discloses that the use of intracellular antigen as preferable over cell surface antigen (e.g. see page 11). Thus, the method of making a B cell antibody taught by the instant specification would encompass any antibody that binds cell surface as well as intracellular proteins not exclusive to B cells (e.g. HLA-DR expressed on B cell and other cell type as taught by Meyer et al.). One of skill in the art would not be able to make the claimed B-cell antibody that specifically binds only B-cells and to use it in the claimed method of ablating normal cells and/or a method of treating an immune disease by administering the antibody produced under guidance of the instant specificaiton.

Therefore, applicant's arguments have not been found persuasive.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 78, 81-86, 102-105, 109-113, and newly added claims 114-116 are rejected under 35 U.S.C. 102(b) as being anticipated by Meyer et al. (US Patent 4,861,579, reference of record) for reasons of record.

The prior Office Action (mailed on April 15, 2009) states:

"*Meyer et al. teach a method of treating immune diseases such as infection, autoimmune disease by administering an anti-B antibody or fragment thereof (see entire document, particularly columns 1-3). Meyer et al. further teach that said antibody can be conjugated with therapeutic agents such as radioisotopes, toxins, cytotoxic agents (e.g. see column 2).*"

Applicant's arguments, filed on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant argues that Meyer et al. only teach two antibodies, Lym-1 and Lym-2, that bind the HLA-DR receptor on B cell surface but these antibodies are not considered bind B-cell specifically. Applicant further argues that Meyer et al. administer the antibodies to alleviate the side effects associated with therapeutic antibody not ablating normal cells as claimed. Thus, applicant asserts that Myer et al. do not anticipate the claimed invention.

This is not found persuasive for following reasons:

Contrary to applicant's reliance on the newly added limitation of "a B cell antibody... which specifically binds to a B-cell" to exclude the antibodies taught by Meyer et al., it is noted that the claimed antibody is interpreted as being an antibody that

binds B-cell as taught by the instant specification. For example, For example, the specification discloses isolation of cell membrane or intracellular antigens to be used to immunize animals to make antibody (e.g. see page 11 of the instant specification). As such and consistent with the prosecution history of the application, the claimed "a B cell antibody... which specifically binds to a B-cell" is read as any antibody that binds to a B-cell antigen specifically the antibody is not read as selectively specific only to B cell. Meyer et al. teach a method of treating immune diseases such as infection, autoimmune disease by administering an anti-B antibody or fragment thereof (see entire document, particularly columns 1-3). Meyer et al. further teach that said antibody can be conjugated with therapeutic agents such as radioisotopes, toxins, cytotoxic agents (e.g. see column 2). Therefore, Meyer et al. meet the claimed limitations. As such, Meyer et al. meet the claimed limitations.

Further, in contrast to applicant's assertion that Meyer et al. only teach Lym-1 and Lym-2 antibodies, it is noted that a prior art must be considered in its entirety, see MPEP 2141.02. In this case, once again, the scope of the prior art teachings are not simply limited to the working examples of Lym-1 and Lym-2. The prior art's method of treating an immune disease by administering anti-B cell antibody encompasses antibody that would read on the instant claims.

Furthermore, regarding applicant's assertion that Meyer et al. do not teach ablating normal cells, it is noted that the instant method encompass a single active step of administering a B-cell antibody. The newly added "thereby to ablate the normal cells" is not considered as an active method step but rather a inherent properties of the B-cell antibody being administered since the thereby clause does not appear to result in a manipulative difference in the method steps when compared to the prior art disclosure. As such, Myer et al.'s antibodies that bind normal B-lymphocytes would inherently result in ablating normal cells including spleen cells in a subject. It is reasonable to conclude that the same patient is being administered the same active agent of B-cell antibody by

the same mode of administration in both the instant claims and the prior art reference. The fact that applicant may have discovered another beneficial effect of ablating normal cells from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 00-1304 (CAFC 4/20/01).

Therefore, applicant's arguments have not been found persuasive.

11. Claims 78, 79, 81, 93, 102-107, 109-113, and newly added claims 114-116 are rejected under 35 U.S.C. 102(b) as being anticipated by Bussel et al. (Blood 1988 72;1:121-127, reference of record) as evidenced by de Grandmont et al. (Blood 2003 101;8:3065-3073, reference of record) for reasons of record.

As stated previously, *"Bussel et al. teach method of treating immune thrombocytopenic purpura by administering intravenous immunoglobulins (IVIG) (see entire document, particularly Material and Methods on pages 121 and 124).*

As evidenced by de Grandmont et al, IVIGs are IgG solutions prepared from pooled plasma of healthy human donors and contain antibodies reacting against a large repertoire of antigens, including those on B lymphocytes (see entire document, particularly page 3065). Therefore, the reference method using IVIG would inherently encompass intact B-cell antibodies.

Further, although the reference is silent about B-cell antibody, it does not mean that the referenced IVIG does not bind epitopes on B-cell. Since the Office does not have a laboratory to test the referenced IVIG, it is applicant's burden to show that the referenced IVIG does not contain B-cell antibodies. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Furthermore, it does not appear that the claim limitation results in a manipulative difference in the methods steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d1508 (CAFC2001). It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable."

Applicant's arguments, filed on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant once again argues that IVIG does not include B-cell antibodies. Applicant argues that the mechanism of action of IVIG is via its interaction of the Fc region. Applicant asserts that even if IVIG contains B-cell antibody, it would not be sufficient to encompass "a therapeutically effective amount" as claimed. Thus, applicant argues the rejection should be withdrawn.

This is not found persuasive for following reasons:

As stated above, the claimed "a B cell antibody... which specifically binds to a B-cell" is read as any antibody that binds to a B-cell antigen specifically. The claimed B-cell antibody is not interpreted as binding selectively to B-cell. Contrary to applicant's assertion, it is again noted that during patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification.". See MPEP 2111. Here, given that the instant specification discloses that antibodies can be made using antigens isolated from cell membrane as well as intracellular proteins (e.g. see lines 5-12 on page 11 of the instant specification), the claimed B-cell antibody includes any antibody that binds proteins on surface of B-cells. Therefore, IVIG that binds B cells are considered B-cell antibody as evidenced by Grandmont et al. that IVIG binds CD40 that is expressed on B-cell. Thus, the anti-CD40 antibody within IVIG is considered specific for CD40, a B cell surface protein. Again, given that no clear definition was given regarding the broadly claimed B-cell antibody as well as applicant's assertion that B-cell antibody meant antibodies targeting B cell antigens (see Interview summary mailed on December 6, 2007), IVIG containing antibodies that bind CD40 expressed on mature B cells is considered B-cell antibody that specifically binds a B-cell.

Further, contrary to applicant's assertion that the IVIG is not administered in "a therapeutically effective amount", it is noted that the claimed therapeutically effective

amount does not define parameter that would exclude the IVIG amount being administered by the prior art. Moreover, Bussel et al. expressly teach repeated infusion of IVIG at 800 to 1000 mg/kg (e.g. see Abstract). Applicant has not provide objective evidence to show that the prior art's administration of the IVIG is not a therapeutically effective amount.

Furthermore, once again, in contrast to applicant's reliance on the mechanism of action of IVIG, it is noted that the mechanism of action disclosed by the prior art does not preclude that the methods and compositions of the prior art IVIG inherently would have had the properties of B-cell antibody recited in the claims because compositions comprising the same type of B-cell antibodies are administered to the same patients to treat the same type of autoimmune disease ITP to achieve the same result.

Therefore, applicant's arguments have not been found persuasive.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 78, 80, 93, 95-101, 107, and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer et al. (US Patent 4,861,579, reference of record) in view of Sivam et al. (US Patent 5,116,944, reference of record) for reasons of record.

The Office Action mailed on July 26, 2007 states:

"The teachings of Meyer et al. have been discussed, supra, in Section 15.

The reference teachings differ from the claimed invention by not describing Fv, , single chain antibody, Fab, Fab', F(ab')$_2$, chimeric antibody, and antibody that is conjugated to cytokine.

However, the advantages of using Fv, Fab, Fab', F(ab')$_2$, chimeric antibody, and antibody that is conjugated to cytokine were well known in the art at the time the invention was made. For example, Sivam et al. teach antibody and its fragments such as Fv, single chain antibody, Fab, Fab', F(ab')$_2$, and chimeric antibody can be conjugated to cytokines to improve characteristic such as serum half-live of cytokines, stability, and receptor mediated uptake for better target delivery (see entire document, particularly columns 5-6). Further, Gowsala et al. teach said antibody conjugates can be used for enhanced therapeutic applications (see column 2, in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use antibody and its fragments conjugated to cytokines in a method of treating an immune disease because anti-B cell antibody can be used in methods of treating immune diseases and antibody and its fragments such as Fv, single chain antibody, Fab, Fab', F(ab')$_2$ can be conjugated to cytokines to improve characteristic for enhanced therapeutic effect."

Applicant's arguments, submitted on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant's arguments and the Examiner's rebuttal regarding the teachings of Meyer et al. are essentially the same as discussed, supra.

Given the teachings of Meyer et al. regarding method of treating an immune disease using anti-B cell antibody, and the teachings of Sivam et al providing methods of making and using antibody and its fragment conjugated with cytokines, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of practicing the claimed method of treating an immune disease by using anti-B cell antibody and its fragments that are conjugated to cytokines.

Therefore, applicant's arguments have not been found persuasive.

14. Claims 78 and 94 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meyer et al. (US Patent 4,861,579, reference of record) in view of Fishwild et al. (Nature Biotech. 1996, 14:845-851, reference of record) for reasons of record.

The Office Action mailed on July 26, 2007 states:

"*The reference teachings differ from the claimed invention by not describing a human monoclonal antibody.*

However, methods of making human monoclonal antibody and its use in therapy were well known in the art at the time the invention was made. For example, Fishwild et al. teach method of making human monoclonal antibodies using transgenic mice carrying human immunoglobulin gene loci; Fishwild et al. further teach that human monoclonal antibody is less immunogenic and have longer half-life in human, thus, more efficacious than murine antibody (see entire document, particularly page 845).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use human monoclonal anti-B cell antibody in a method of treating an immune disease because anti-B cell antibody can be used in methods of treating immune diseases and antibody and human monoclonal antibody is more efficacious in human."

Applicant's arguments, submitted on October 15, 2009, have been fully considered but have not been found persuasive.

Applicant's arguments and the Examiner's rebuttal regarding the teachings of Meyer et al. are essentially the same as discussed, supra.

Given the teachings of Meyer et al. regarding method of treating an immune disease using anti-B cell antibody, and the teachings of Fishwild et al. providing methods of making and using human monoclonal antibody, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success of practicing the claimed method of treating an immune disease by using human monoclonal anti-B cell antibody.

Therefore, applicant's arguments have not been found persuasive.

15. Conclusion: no claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Dahle whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Ram Shukla can be reached 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Dahle
Patent Examiner
February 17, 2010

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644